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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,695	01/28/2002	Samuel J. Danishefsky	2003080-0089	5540

24280 7590 04/16/2002

Choate, Hall & Stewart  
Exchange Place  
53 State Street  
Boston, MA 02109

EXAMINER

SOLOLA, TAOFIQ A

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 04/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
10/058,695

Applicant(s)  
Danishefsky et al.

Examiner  
Taofiq A. Solola

Art Unit  
1626



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Jan 28, 2002
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 59-95 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 59-95 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:

- ☐ Certified copies of the priority documents have been received.
- ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_
- ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4 20) ☐ Other:

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***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 87-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing apoptosis (cell death) of cancer or tumor cells, does not reasonably provide enablement for their “inhibition”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The asserted utility is not believable on it’s face. There is no known epothilone for the inhibition of cancer or tumor cells, and the specification does not provide sufficient enabling disclosure for the claimed utility.

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988):

- 1) Breadth of claims.
- 2) Nature of invention.
- 3) State of prior art.
- 4) Level of ordinary skill in the art.
- 5) Level predictability in the art.

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6) Amount of direction and guidance provided by the inventor.

7) Existence of working examples.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breath of the claimed invention involve the use of epothilones. The nature of the invention is in the field of medicinal chemistry wherein, applicant is claiming the methods of use of epothilones for the "inhibition" of cancer or tumor cells.

The state of the prior art is what prior art knows about the nature of the invention. There is no known prior art claiming the inhibition of cancer or tumor cells by epothilones. The level of ordinary skill in the art is high but, only in the art of inducing apoptosis of cancer or tumor cells. The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. The lower the predictability, the higher the direction and guidance that must be provided by applicant. In the instant invention the predictability is very low and consequently, the need for higher levels of direction and guidance by applicant. However, the amount of direction and guidance provided by applicant is limited to assays involving only the induction of apoptosis in cancer or tumor cells. There is no evidence in the specification that established correlation between the experiments and inhibition of cancer or tumor cells. See Ex parte Mass, 9 USPQ2d 1746, 1987. The quantity of experimentation required to use the the compounds as claimed in the instant invention, based on applicants limited disclosure would be undue burden because, one of

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ordinary skill in the art would have to perform significant amount of in-vivo experiments as well as additional in-vitro assays. By deleting "inhibition" from the claims, the rejection would be overcome.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 87-95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "killing," line 1, and "kill," line 3, claim 87 and line 2, claim 95, are not consistent with induction of apoptosis by epothilone. Therefore, claims 87-95 are indefinite. By replacing the terms with "apoptosis" the rejection would be overcome.

The term "anticancer agent," line 1, claim 63, lacks proper antecedent basis in claim 59. Therefore, claims 63 is indefinite.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 59-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bollag et al., Cancer Res., Vol. 55 (1995), pages 2325-2333.

Applicants claim composition of epothilone and methods of use for treating cancer or tumors particularly drug-resistant cells. In preferred embodiments, the composition further comprises at least one cytotoxic agent. Applicants also claim effective amounts of epothilones from 0.001 to 40 mg/kg of body weight.

Determination of the scope and content of the prior art (MPEP §2141.01)

Bollag et al., teach epothilones A and B, their compositions as oily residue (column 2, page 2326) and methods of use for treating cancer or tumor cells and particularly multiple drug-resistant cells. See column 2, page 2331. Bollag et al., also teach the method of use of epothilones in combination with taxol (a cytotoxic agent). See column 2, page 2328 to column 1, page 2330.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant invention and that of Bollag et al., is that applicants are claiming effective amounts of epothilones from 0.001 to 40 mg/kg of body weight.

Finding of prima facie obviousness---rational and motivation (MPEP §2142.2413)

However, for Bollag et al., to use epothilones for the treatment of cancer or tumors, effective amount must necessarily be used. Also, claiming effective amounts of epothilones from 0.001 to 40 mg/kg of body weight, is not in and of itself patentable over the prior art of

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Bollag et al. Therefore, the instant invention is prima facie obvious from the teaching(s) of

Bollag et al. The motivation is to make additional epothilone composition useful for the treatment of cancer.

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### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 59-95 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 30, 59-93 of copending Application No. 09/874,514. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

### ***Objection***

Claims 59 and 60 are objected to because they are duplicates. Claim 59 is drawn to a composition which inherently must comprise a pharmaceutically acceptable carrier or diluent. By deleting one of the claims the rejection would be overcome.

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*Specification*

Pages 76 and 86 of the specification are missing the last ~~1~~2 lines. Also, brief description of figures 20B and 20C are not disclosed in the specification.

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*Telephone Inquiry*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Taofiq A. Solola whose telephone number is (703) 308-4690. The examiner is on flexible work schedule and the best days to get him are Mondays, Wednesdays and Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (703) 308-4537. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.



Taofiq A. Solola, Ph.D.  
Primary Examiner  
Group 1626

April 12, 2002





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Bib Data Sheet

CONFIRMATION NO. 6697

<b>SERIAL NUMBER</b> 09/874,514	<b>FILING DATE</b> 06/05/2001 <b>RULE</b>	<b>CLASS</b> 514	<b>GROUP ART UNIT</b> 1626	<b>ATTORNEY DOCKET NO.</b> 2003080-0082 (SK-744-CON3)
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**\*\* CONTINUING DATA \*\*\*\*\***

THIS APPLICATION IS A CON OF 08/986,025 12/03/1997 PAT 6,242,469  
 WHICH CLAIMS BENEFIT OF 60/032,282 12/03/1996  
 AND CLAIMS BENEFIT OF 60/033,767 01/14/1997  
 AND CLAIMS BENEFIT OF 60/047,566 05/22/1997  
 AND CLAIMS BENEFIT OF 60/047,941 05/29/1997  
 AND CLAIMS BENEFIT OF 60/055,533 08/13/1997

**\*\* FOREIGN APPLICATIONS \*\*\*\*\***

**IF REQUIRED, FOREIGN FILING LICENSE GRANTED**  
**\*\* 06/28/2001**

Foreign Priority claimed <input type="checkbox"/> yes <input type="checkbox"/> no	<b>STATE OR COUNTRY</b> NJ	<b>SHEETS DRAWING</b> 76	<b>TOTAL CLAIMS</b> 58	<b>INDEPENDENT CLAIMS</b> 24	
35 USC 119 (a-d) conditions met <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> Met after Allowance.					
Verified and Acknowledged	Examiner's Signature	Initials			

**ADDRESS**  
24280

**TITLE**  
Synthesis of epothilones, intermediates thereto, analogues and uses thereof

<b>FILING FEE RECEIVED</b> 2950	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	<input type="checkbox"/> All Fees
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